

Applicant : BIANCHI, et al.
U.S. Serial No. : Not Yet Known
Filed : Herewith
Page : 2

In The Claims:

Please amend claims 6-9 and 14-15 without prejudice to the applicants' rights to pursue the amended subject matters in a future application.

1. (Original) A composition comprising an effective amount of the HMGB1 protein or functional parts thereof, or HMGB1 expressing vectors, for the treatment of tissue damage and/or to promote tissue repair and regeneration.
2. (Original) Composition according to claim 1 wherein the tissue regeneration depends from the growth of cells of the same type as those damaged, excluding connective tissue.
3. (Original) Composition according to claim 2 wherein the tissue is cardiac or skeletal muscle.
4. (Original) Composition according to claim 3 wherein the tissue repair and/or regeneration includes the repair and/or regeneration of areas of necrosis.
5. (Original) Composition according to claim 4 wherein the areas of necrosis comprise trauma sites, ischemia sites including infarcted heart, burn sites.
6. (Currently Amended) Composition according ~~to any of~~ previous claims 1 further comprising an effective amount of an anti-inflammation agent.
7. (Currently Amended) Composition according ~~to any of~~ previous claims 1 further comprising diluents and/or adjuvants for perfusion at the tissue repair site.

Applicant : BIANCHI, et al.
U.S. Serial No. : Not Yet Known
Filed : Herewith
Page : 3

8. (Currently Amended) Composition according to ~~any of previous~~ claims 1 further comprising diluents and/or adjuvants and/or carriers for intramuscular injection.
9. (Currently Amended) Composition according to ~~any of previous~~ claims 1 further associated to stem cells.
10. (Original) Composition according to claim 9 wherein said stem cells are mesoangioblasts.
11. (Original) A composition comprising an effective amount of an antagonist of the HMGB 1 protein for the treatment of adverse effects induced by necrotic tissue, such as activation of nearby surviving cells, the recruitment and activation of myeloid cells, loss of the barrier function of endothelia, edema.
12. (Original) Composition according to claim 11 wherein the necrotic tissue refers to intestinal infarction, acute pancreatitis and extensive trauma.
13. (Original) Composition according to claim 12 wherein the adverse effects Induced by necrotic tissue include long term effects of necrosis, such as sepsis and multiple organ failure.
14. (Currently Amended) Composition according to claims ~~11 to 13~~ wherein the HMGB1 antagonist comprises HMGB 1 antibodies and functional recombinant or Synthetic

Applicant : BIANCHI, et al.
U.S. Serial No. : Not Yet Known
Filed : Herewith
Page : 4

portions thereof, interference RNAS, antisense RNAS, synthetic or natural modulators.

15. (Currently Amended) Composition according to claims 11 to 14 wherein the composition is administered within 16 hours of the necrotic event.
16. (Original) Method to promote stem cell migration AND/OR proliferation in cell culture or in vivo comprising the step of exposing such cells to an effective amount of the HMGB1 protein or functional parts thereof.
17. (Original) Method according to claim 16 wherein said stem cells are resident cardiac or circulating stem cells.
18. (Original) Method to promote the proliferation of cardiomyocytes in cell culture or in vivo comprising the step of exposing such cells to an effective amount of the HMGB1 protein or functional parts thereof.

Applicant : BIANCHI, et al.
U.S. Serial No. : Not Yet Known
Filed : Herewith
Page : 5

On page 33, please add the below paragraph starting on line 1:

**USE OF HMGB1 IN THE TREATMENT OF TISSUE DAMAGE AND/OR TO
PROMOTE TISSUE REPAIR**

ABSTRACT OF THE INVENTION

-It is described a composition comprising an effective amount of the HMGB1 protein or functional parts thereof, of HMGB1 expressing vectors, for the treatment of tissue damage and/or to promote tissue repair and regeneration. It is further described a composition comprising an effective amount of an antagonist of the HMGB1 protein for the treatment of adverse effects induced by necrotic tissue, such as recruitment and activation of myeloid cells, loss of the barrier function of endothelia, edema.-